

Claims :

1. A process for the preparation of Gabapentin Form-II comprising steps:

- Reaction of the 1,1-cyclohexane di acetic acid mono amide with alkali hypo halite solution at temperature of about -10^0C to about 5^0C , followed by acidification with sulphuric acid in presence of an organic solvent-1
- Extraction of the formed sulphate salt with organic solvent-2
- Separation of the organic layer, drying over dehydrating agents
- Addition of an ante solvent to precipitate the hemisulphate hemihydrate salt followed by its isolation
- Dissolution of the hemisulphate hemihydrate salt in a short chain alcohol
- Separation of the insolubles if any
- Neutralization of the filtrate with base at temperature of about 70^0C to liberate the free amino acid
- Isolation of the liberated free amino acid by cooling, leaving the formed byproduct base-salt in the mother liquor / solvent
- Separation of the formed Gabapentin Form-II
- Purification of the product by slurring in ethanol at temperature of about 60^0C - 70^0C
- Recovery of the final product by filtering and drying

to obtain Gabapentin Form-II having sulphate ions less than 100 ppm with respect to Gabapentin.

25 2. A process as claimed in claim 1, wherein the organic solvent-1 is selected from n-Butanol, MIBK, methyl ethyl ketone and THF, the preferred solvent being n-Butanol

30 3. A process as claimed in claim 1, wherein the organic solvent-2 for extraction of hemi sulphate hemihydrate salt is n-Butanol, MIBK, THF and methyl ethyl ketone, the prefferred solvent being n-Butanol

4. A process as claimed in claim 1, wherein drying of organic layer is carried out over dehydrating agents such as anhydrous sodium sulphate and anhydrous magnesium sulphate and anhydrous calcium sulphate the preferred ones being anhydrous sodium sulphate or anhydrous magnesium sulphate
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5. A process as claimed in claim 1, wherein the ante solvent is selected from acetone, toluene, n-hexane, and Di isopropyl ether
- 10 6. A process as claimed in claim 1, wherein the short chain alcohol is ethanol and n-Butanol
7. A process as claimed in claim 1, wherein the base is selected from Di isopropyl ethylamine, triethylamine
- 15 8. A process as claimed in claim 1, wherein the neutralization temperature is in the range of 65⁰C - 75⁰C
9. A process as claimed in claim 1, wherein purification of Gabapentin is done by slurring in ethanol in the temperature range 65⁰C - 70⁰C
- 20 10. Crystalline Gabapentin hemisulphate hemihydrate characterized by powder x-ray diffraction peaks at 2-theta 6.8, 13.7, 17.0, 18.0, 20.2, 20.6, 24.2, 24.6, 26.2, 26.8, 27.7, 29.9, 30.8, 34.0, and 34.7 degrees.
- 25 11. Crystalline Gabapentin hemisulphate hemihydrate characterized by infra-red absorptions having peaks at 686, 757, 901, 917, 986, 1127, 1142, 1200, 1282, 1315, 1430, 1462, 1525, 1580 and 1714 cm⁻¹.

12. A process for the preparation of Gabapentin hemisulphate hemihydrate comprising steps:

- Reaction of the 1,1-cyclohexane di acetic acid mono amide with alkali hypo halite solution at temperature of about -10°C to about 5°C , followed by acidification with sulphuric acid in presence of an organic solvent-1
- 5 - Extraction of the formed sulphate salt with organic solvent-2
- Separation of the organic layer, drying over dehydrating agents
- Addition of an ante solvent to precipitate the hemisulphate hemihydrate salt followed by its isolation
- Isolation of the Gabapentin hemisulphate hemihydrate
- 10 - Drying of the Gabapentin hemisulphate hemihydrate

13. A process as claimed in claim 1, wherein the organic solvent-1 is selected from n-Butanol, MIBK, methyl ethyl ketone and THF, the preferred solvent being n-Butanol

15 14. A process as claimed in claim 1, wherein the organic solvent-2 for extraction of hemi sulphate hemihydrate salt is n-Butanol, MIBK, THF and methyl ethyl ketone, the prefferred solvent being n-Butanol

20 15. A process as claimed in claim 1, wherein drying of organic layer is carried out over dehydrating agents such as anhydrous sodium sulphate and anhydrous magnesium sulphate and anhydrous calcium sulphate the preferred ones being anhydrous sodium sulphate or anhydrous magnesium sulphate

25 16. A process as claimed in claim 1, wherein the ante solvent is selected from acetone, toluene, n-hexane, and Di isopropyl ether

17. Drying of the Gabapentin hemisulphate hemihydrate in a temperature range $50-60^{\circ}\text{C}$

30 18. A process as claimed in claims 1 – 12 for the preparation of Gabapentin form-II via the Gabapentin hemisulphate hemihydrate.